

AMENDMENTS TO THE DRAWINGS

Figure 1 in Drawing Sheet 1 is amended. The attached Annotated Drawing Sheet 1 shows the amendments made.

Figure 3 in Drawing Sheets 4-70 is amended. The attached Annotated Drawing Sheets 4-70 show the amendments made.

Applicants also provide Replacement Drawing Sheets 1 and 4-82 which replace the original Drawing Sheets 1 and 4-82.

REMARKS/ARGUMENTS

Claims 2, 3, 7, 8, 10, 11, 16, 17 and 19-26 are being cancelled. Claims 1, 4, 9, 12-15 and 18 are being amended. New claims 27-29 are being added. No new matter has been introduced by the amendments.

After entry of the above amendments, claims 1, 4-6, 9, 12-15, 18 and 27-29 will be pending.

Election/Restrictions

The Examiner issued a telephonic restriction, where the claims were divided into Group I (claims 1-18) and Group II (claims 19-26). Pursuant to 37 C.F.R. § 1.142 and in response to Examiner's telephonic restriction, Applicants provisionally elected Group I (claims 1-18) without traverse. Applicants hereby affirm the provisional election.

Applicants note that the Official Action indicates that the Examiner is withdrawing claims 11-15 from further consideration because those claims are drawn to non-elected subject matter. However, claims 11-15 are part of the Group I claims and, accordingly, pertain to elected subject. Applicants believe that claims 11-15 have been withdrawn by the Examiner in error. Instead, claims 19-26 should have been withdrawn. The attached Listing of the Claims reflects Applicants understanding by indicating that claims 19-26 are being cancelled. Applicants request further clarification should our understanding be incorrect.

Applicants reserve the right pursuant to 35 U.S.C. § 121 to file one or more divisional applications directed to the non-elected subject matter during the pendency of the present application.

Non-Compliance with Sequence Rules

Paragraphs [0189]-[0190] are being amended to clarify that CatS as used in those paragraphs refers to SEQ ID No: 3, as suggested by the Examiner.

Paragraphs [0041], [0042], [0043], [0044], [0046] and the headings of Tables 2-8 are similarly being amended to clarify that CatS as used in those paragraphs refers to the catalytic domain of CatS (residues 115-331 of SEQ. ID No: 1).

Objections to the Specification

The Specification is being amended at paragraph [0056] to clarify that E-64 refers to L-*trans*-epoxysuccinyl-leucylamido(4-guanidino)butane. E64 would have been known to persons skilled in the art at the time the present invention was made as an inhibitor of cysteine proteinases (*see, e.g., Barrett et al., Biochem. J. (1982) 201, 189-198; copy attached*).

Paragraph [0097] is being amended to correct a clerical error by replacing “□L” with “μL.”

In view of the foregoing, the objections to the Specification should be withdrawn.

Objections to the Drawings

Figure 1 is being amended to replace the sequence of SEQ ID NO: 2 with the full cDNA sequence for CatS, as suggested by the Examiner. SEQ ID NO: 2 can be found at GenBank Accession No. NP 004079; Wiederanders, B *et al.* “Phylogenic conservation of cysteine proteinases: Cloning and expression of a cDNA coding for human cathepsin S.” *J. Biol. Chem.*, 267, 13708-13 (1992), which is incorporated by reference at paragraph [0051]. Applicants note that Figure 1 is also being amended to underline residues 115-331 of SEQ ID No. 1, as recited in the description of SEQ ID No. 1. Accordingly, the objection to the figures should be withdrawn.

Rejections under 35 USC §112, First Paragraph

The Examiner rejects claims 1-15 under 35 U.S.C. §112, First Paragraph, on the ground that the claims, as presented, do not satisfy the written description or enablement requirements.

Applicants are amending the claims such that all the pending claims are drawn to compositions and methods utilizing SEQ. ID No. 3 which is shown in Figure 1.

In view of the above amendments, Applicants submit that the pending claims overcome the Examiner's rejections. Withdrawal of the rejections to these claims under 35 U.S.C. §112, First Paragraph, is respectfully requested.

Rejections under 35 U.S.C. §102

Claims 16 and 17 are being cancelled thereby rendering the rejection under 35 U.S.C. §102 moot.

Additional Amendments of the Specification

Paragraph [0056] is being amended to correct certain inadvertent clerical errors.

Paragraph [0077] is being amended to reflect that SEQ ID No. 2 relates to the portion of the gene encoding amino acid residues 1-331 of SEQ ID No. 1.

Paragraph [00125] is being amended to reflect that the refined crystal structure of CatS-E64 contains residues 114-331 of SEQ ID No. 1.

Paragraph [00187] is being amended to reflect that the portion of the gene encoding residues 114-331 of SEQ ID No. 1 was amplified and cloned into a vector with a Glycine-6x-histidine tag. Paragraph [00187] is also being amended to delete the reference to SEQ ID No. 2 in Figure 1.

Paragraph [00188] is being amended to recite that expression of the described vector generates a fusion protein containing CatS residues 114-331 of SEQ ID No. 1 with a C-terminal Glycine-6x-histidine tag. Paragraph [00188] is also being amended to reflect that the amino acid sequence of the fusion protein is given in SEQ ID No. 3.

Paragraph [00191] is being amended to recite that residues 114-331 of CatS with a C-terminal Glycine-6x-histidine tag (SEQ ID No. 3) were incubated.

No new matter is being added by these amendments

Additional Amendments of the Claims

Claim 9 and 12-15 are being amended to provide antecedent basis for the protein crystal.

Claims 4 and 12 are being amended to clarify that the claims relate to the X-ray determination of structure coordinates to a resolution of a value equal to or less than 3.0 Angstroms, which is a higher resolution.

Claim 18 is being amended to relate to a protein consisting of SEQ ID No. 3.

Additional Amendments to the Drawings

Figure 3 is being amended to make the amino acid numbers of column E conform to the corresponding residue numbers of SEQ. ID No. 3.

Substitute Sequence Listing

Applicants submit the enclosed Substitute Sequence Listing in order to replace SEQ ID No. 2 with the cDNA sequence for full-length Cathepsin S; label certain features of SEQ ID Nos. 1-4; and identify the species of SEQ ID Nos. 3 and 4 as Artificial. No other amendments relative to the original sequence listing are made in the Substitute Sequence Listing.

Two copies of the Substitute Sequence Listing in written form are enclosed. A CD-R containing the Substitute Sequence Listing in computer readable form (CRF) is also enclosed.

Pursuant to 37 C.F.R. §1.821(f) and (g), I hereby state that the information recorded in computer readable form on the enclosed CD-R is identical to the written Substitute Sequence Listing enclosed herein for the above-referenced application. I hereby further state that the submission, filed in accordance with 37 C.F.R. §1.821(g), herein does not include new matter.

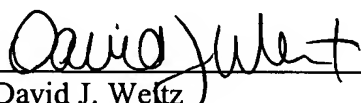
CONCLUSION

In light of the amendments and remarks set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance.

Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,
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